Remarks

Objection to the Priority Claim

Applicants have amended the specification to include the issued patent number and issue date, to which priority is claimed.

Objections to the Specification

The Examiner objected to the specification for containing trademarks without the proper trademark symbol and generic name. Applicants have amended the specification to include trademark registration symbols and generic equivalents where necessary.

Restriction Requirement

The Examiner made the restriction requirement mailed on October 5, 2006, final but in so doing the Examiner changed which claims were included in Group III. In the Office Action mailed on October 5, 2006, the Examiner restricted claims 22-49 and 69-70 into Group III. Applicants elected Group III with traverse in the response filed on April 2, 2007. If Group III were elected, the Examiner also required the election of one species of bacterial cell from claims 22 or 69 and one species of genes from claims 28 or 30 for prosecution on the merits. Applicants further elected *Salmonella spp.* and *sse* genes for prosecution on the merits. When making the restriction requirement final, the Examiner limited Group III to claims 22-29, 35-40, and 43-49. At a minimu, claim 30 should be rejoined to Group III because claim 30 identifies specific *sse* genes targeted for inactivation. Additional claims should also be rejoined in view of the amendments to modify dependency to those claims which are in the elected group.

Double Patenting

Claims 22-29, 35-40, and 43-49 were rejected under 35 U.S.C. § 101 based on double patenting of the same invention in view of claims 22-29, 35-40 and 43-49 of U.S. Patent Application No. 10/007,463. Applicants respectfully traverse the rejection.

U.S. Patent Application No. 10/007,463 is abandoned and cannot be used as the basis for a rejection of the pending claims for double patenting.

Rejections under 35 U.S.C. § 101

Claims 22-29, 35-40, and 43-49 were rejected under 35 U.S.C. § 101 as not being patentable subject matter. Solely to expedite prosecution, Applicants have amended the claims as suggested by the Examiner to be directed to an "isolated" gram-negative *Salmonella* cell.

However, the examiner is incorrect. The attenuated strains do not exist in nature. 35 U.S.C. 101 prohibits claims to naturally occurring bacteria, but as repeatedly affirmed by the U.S. Supreme Court and the Court of Appeals for the Federal Circuit, one can claim any bacteria that has been altered by the hand of man. It is not necessary to claim an isolated organism if the organism is not naturally occurring, in order to comply with 35 U.S.C. 101. The examiner has presented no evidence of art showing that the claimed mutations occur in nature.

Rejections under 35 U.S.C. § 112, first paragraph, biological deposit

Claim 27 was rejected under 35 U.S.C. § 112, first paragraph as not described in the specification as in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed subject matter at the time the application was

filed. Applicants respectfully traverse the rejection to the extent it is applied to the claims as amended.

Legal Standard

Where an invention is, or relies on, a biological material, the disclosure may include reference to a deposit of such biological material. 37 C.F.R. § 1.802. ***Biological material need not be deposited unless access to such material is necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. § 112. Biological material need not be deposited, inter alia, if it is known and readily available to the public or can be made or isolated without undue experimentation.***

Analysis

The Examiner rejected claim 27 because the claimed subject matter allegedly employs novel bacterial strains that were allegedly not publicly deposited. *Salmonella* serotype *typhimurium* Definitive Type 104 (DT104) has been deposited with the American Type Culture Collection of Type Cultures under catalogue number 700408, and is also available from the National Collection of Type Cultures in the UK as Strain No. NCTC 13348. This strain of bacteria was publicly available prior to the priority date of the above-referenced application. See for example, Harnett, N. et al. *Can Commun Dis Rep*, 24⊗3):20-23 (1998) and Poppe, C. et al. *Can Vet J*, 39:559-565 (copies attached). Harnett et al. disclose on page 1 that *S. typhimurium* isolates were submitted to the Central Public Health Laboratory from private community-based laboratories which provide services to physicians, nursing homes, clinics and hospitals across Ontario. Poppe et al. disclose that *Salmonella* DT104 has been isolated from humans and animals in the United Kingdom and several other European countries. This article contains

numerous references to other articles discussing *Salmonella* DT104. Thus, *Salmonella* DT104 was known and readily available to the public prior to the filing of the above-referenced application, and a biological deposit is not required to satisfy 35 U.S.C. § 112, first paragraph. It should be noted, however, that these are the starting materials, not the claimed materials having been modified.

Rejections under 35 U.S.C. § 112, first paragraph, written description

Claims 22-29, 35-40 and 43-49 were rejected under 35 U.S.C. § 112, first paragraph as failing to satisfy the written description requirement. Applicants respectfully traverse the rejection to the extent it is applied to the claims as amended.

Legal Standard

The first paragraph of Section 112 provides that the "specification shall contain a written description of the invention..." 35 U.S.C. § 112 (2007). "The description requirement's purposes are to assure that the applicant was in full possession of the claimed subject matter on the application filing date and to allow other inventors to develop and obtain patent protection for later improvements and subservient inventions that build on applicant's teachings." 3-7 Chisum on Patents § 7.04 (2007), citing *Fields v. Conover*, 443 F.2d 1386, 170 U.S.P.Q. 276 (CCPA 1971).

The general standard for the written description requirement is that "a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." *See* M.P.E.P. § 2163(I). Possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in

detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Id.*, citing *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000); *Pfaff v. Wells Electronics, Inc.*, 55 U.S. at 66, 119 S.Ct. at 311, 48 USPQ2d at 1646. As noted in a recent decision by the Board of Appeals and Interferences, the written description requirement does not require a description of the complete structure of every species within a chemical genus. (*see Utter v. Hiraga*, 845 F.2d 993, 998, 6 U.S.P.Q.2d 1709, 1714 (Fed. Cir. 1988), stating "A specification may, within the meaning of 35 U.S.C. § 112, para. 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.").

A specification may describe an actual reduction to practice by showing that the inventor constructed *an embodiment* or performed *a process* that met all the limitations of the claim and determined that the invention would work for its intended purpose. *Cooper v. Goldfarb*, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998) (emphasis added). Although reduction to practice often provides the best evidence that an invention is complete, actual reduction to practice is not required by the written description requirement. An applicant may show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.

Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In *Falkner*, the Federal Circuit recently addressed the issue of written description in an appeal from an interference. *Falkner v. Inglis*, 448 F.3d 1357, 79 USPQ2d 1001 (Fed. Cir. 2006). The issue was whether the applicant's priority applications adequately described and enabled a poxvirus-based vaccine. The Federal Circuit reiterated that "[t]he 'written description requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves to demonstrate that the patentee was in possession of the invention that is claimed." *Falkner* at 1366. The Federal Circuit also clarified that with regard to the written description requirement: (1) examples are not necessary to support the adequacy of the a written description; (2) the written description standard may be met even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure. *Falkner* at 1366.

With respect to original claims, the M.P.E.P. states that "there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." M.P.E.P. § 2163(I) (A), *citing In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976).

Analysis

The Examiner rejected the claims as failing to satisfy the written description requirement because the scope of the claims includes numerous structural variants of any gram negative cell having any mutation in any locus of SPI2. Solely to expedite

prosecution, Applicants have amended independent claim 22 to be directed to an isolated gram negative *Salmonella* cell wherein at least one *sse* gene is inactivated. Basis for the amendment is found in the specification as originally filed, for example claim 23 and the Examples. The nucleic acid sequences for sse genes is provided in the specification at least at page 84. The paragraph spanning pages 13 and 24 of the specification describe that the mutation can be a deletion, preferably a deletion of at least six nucleotides, and more preferably a deletion of the partial or complete coding sequence for the gene. The specification also discloses that the mutation can be an insertion of a heterologous nucleic acid molecule into the gene to be inactivated, or a combination of deletions and insertions. Thus, one of skill in the art would recognize that the applicants were in full possession of the claimed subject matter on the application filing date, and the rejection should be withdrawn.

Rejections Under 35 U.S.C. § 102

Claims 22, 24, 25 and 26 were rejected under 35 U.S.C. § 102(b) as anticipated by Hensel et al. (Journal of Bacteriology, 179(4):1105-1111 (1997)). Claims 22, 24-26, 35, 38-40, and 44-49 were rejected as anticipated by Shea et al. (Proc. Natl. Acad. Sci. USA, 93:2503-2597). Claims 22-26, 28, 29, 35, 37-40, 44-46, and 49 were rejected as anticipated by Deiwick et al. (Journal of Bacteriology, 180(18):4775-4780). Applicants respectfully traverse the rejections to the extent they are applied to the claims as amended.

Legal Standard

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal*

Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Analysis

Hensel et al. and Shea et al.

Claim 22 was amended to incorporate the elements of claim 23. Applicants note that claim 23 was not rejected as anticipated by Hensel et al. or by Shea et al. Because amended claim 22 incorporates the elements of claim 23, amended claim 22 is novel over Hensel et al. and Shea et al., and the rejections should be withdrawn. Claims 24-26 depend from amended claim 22 and are novel over Hensel et al. and Shea et al. for at least the reasons amended claim 22 is novel over Hensel et al. and Shea et al.

Deiwick et al.

Deiwick et al. is not available as prior art against the above-referenced application, and therefore, cannot anticipate the claimed subject matter. Applicants attach the Declaration under 37 C.F.R. 1.132 of Dr. Darren R. Ritsick who testifies that he contacted the Cushing/Whitney Medical Library at Yale University who advised him that the library received Deiwick et al. (Journal of Bacteriology, 180(18):4775-4780) on September 21, 1998. (see Exhibit A of Dr. Ritsick's Declaration). Dr. Ritsick also testifies that he contacted the Welch Medical Library at Johns Hopkins Medical Institutes who advised him that the library received Deiwick et al. (Journal of Bacteriology, 180(18):4775-4780) on September 14, 1998 (see Exhibits B and C of Dr. Ritsick's Declaration). In view of Dr. Ritsick's declaration, Deiwick et al. was not publicly available until after the earliest effective filing date (September 4, 1998) for the above-

referenced application. Accordingly, Deiwick et al. is not available as prior art, and the rejection should be withdrawn.

Even if Diewick et al. were considered to be prior art, Diewick et al. fails to disclose attenuated mutants in which an *sse* gene has been inactivated. Applicants draw the Examiner's attention to Tables 1 and 2 from which it can be seen that mutations in *sse* genes are not disclosed.

Rejections Under 35 U.S.C. § 103

Claims 22, 40, and 43 are rejected under 35 U.S.C. § 103 as obvious over Deiwick et al. in view of Tsolis et al. (Infection and Immunity, 63(5):1739-1744 (1995). Applicants traverse this rejection to the extent it is applied to the claims as amended.

Legal Standard

Obviousness is a legal conclusion based on underlying facts of four general types, all of which must be considered by the examiner: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any objective indicia of nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459 (1966). This standard was recently affirmed by the Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007).

The Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a). Indeed, the examiner's attention is drawn to the following quote by the Court in *KSR*:

"The TSM test captures a helpful insight: A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art. Although common sense directs caution as to a patent application claiming as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the art to combine the elements as the new invention does. Inventions usually rely upon building blocks long since uncovered, and claimed discoveries almost necessarily will be combinations of what, in some sense, is already known. . . . There is no necessary inconsistency between the test and the *Graham* analysis."

"Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness." *Gillette Co. v. S.C. Johnson & Sons, Inc.*, 919 F.2d 720, 724, 16 U.S.P.Q.2d 1923 (Fed. Cir. 1990); *see Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383, 231 U.S.P.Q. 81, 93 (Fed. Cir. 1986). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures on the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988).

The Court also warned against the use of hindsight analysis in making an obviousness determination. The Court stated, "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." (*KSR*, 127 S. Ct. at 1742, citing *Graham* , 383 U.S. at 36 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and

instructing courts to "'guard against slipping into the use of hindsight'" (quoting *Monroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.*, 332 F.2d 406, 412, 141 U.S.P.Q. 549 (6th Cir. 1964))).

References relied upon to support a rejection under 35 U.S.C. § 103 must provide an enabling disclosure, i.e., "they must place the claimed invention in the possession of the public." *Application of Payne*, 606 F.2d 303, 314, 203 U.S.P.Q. 245 (C.C.P.A. 1979); *see Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 13 U.S.P.Q.2d 1301 (Fed. Cir. 1989). A publication that is insufficient as a matter of law to constitute an enabling reference may still be relied upon, but only for what it discloses. *See Reading & Bates Constr. Co. v. Baker Energy Resources Corp.*, 748 F.2d 645, 651-652, 223 U.S.P.Q. 1168 (Fed. Cir. 1984); *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569 (Fed. Cir. 1991).

Analysis

As discussed above, Deiwick et al. is not prior art, and even if it were considered prior art, it does not disclose or suggest attenuated strains of *Salmonella* having at least one *sse* gene inactivated. Tsolis et al. does not cure this deficiency. Tsolis et al. is cited disclosing superoxide dismutase genes of *Salmonella typhinmurium*. Because Deiwick et al. is not prior art and because the combination of Deiwick et al. and Tsolis et al. does not disclose or suggest each element of the claims, the rejection should be withdrawn.

Status of the Claims

Applicants acknowledge with thanks that claims 27 and 36 are free of the prior art.

Allowance of claims 1-16, 22, 26, 27, 30-49, 69-70 and 91-98 is respectfully requested.

Respectfully submitted,

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